# Persian Gulf Illness Update--2004

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# PGI--History

- 2 Aug, 1990:  Iraq invades Kuwait
- 8 Aug: first elements of 82nd ABN arrive, Saudi Arabia
- Desert Shield (Aug 90-Jan 91)--Coalition forces build up to defend Arab states; take back Kuwait
- Bombings, 6 weeks, Jan-Feb 1991

# PGI--History

- By time of 4 day war, Feb 1991, 700K U.S. troops (7% women; 200K/700K Reserve/NG)
- Incoming SCUDS, with damage/death; great fear of chem/bio weapons (Iraqi intentions borne out post war). Uncertain use or exposure to chem agents (experienced chem war poohbahs: you’re kidding)
- Most troops return by May 1991

# PGI--History

- By 1992, rumors of ?excess illness in PG vets circulating.
- 1992--VA opens Persian Gulf Registry
- 1994--MMWR report of ? excess illness (self-report)
- 1994--DOD initiates CCEP program; by 1 y later, has evolved into 2 stage program familiar now (1st stage screen; 2nd stage referral, with esp neuro, pulm, ID, psych, GI and derm evals). Parallel data to VA program

# PGI--History

- By 1994--disability offered to any vet with chronic disabling, even if unexplained sx.
  - (? Political grandstanding?:  Same has occurred in every war back to WWI)

# PGI--Definition

Still can’t be done.

# PGI--Features

- Myriad of symptoms, in various combos in any 1 patient
  - Excessive fatigue
  - Neurobehavioral/cognitive manifestations
  - HA
  - Joint/muscle pains
  - Sensory sx
  - Diarrhea

# PGI--Features

- (Symptoms, cont.)
  - Respiratory sx
  - GI sx
  - Musculoskeletal sx
  - Derm sx
- Illness in spouses
- Birth defects in offspring

# PGI--CCEP data*

- 20,000 participants by 1997 (no new/changed data since)
- As primary diagnosis: %
  - Dz of muscle/connective tissue 18
  - Mental disorders 18
  - Signs, sx, ill-defined conditions 18
  - Dz of resp system 7
  - Dz of skin/soft tissue 6
  - Dz of nervous system/sense organs 6
  - Rest: <2.5 % each

** Joseph, Mil Med, 1997. No diff from VA PGR data*

# PGI--CCEP data

- Sx, signs, ill-defined conditions: most frequent sx, patients with any c/o:
  - Fatigue 60 %
  - Joint pain/muscle pain 47/22
  - HA 44
  - Memory problem 40
  - Sleep disturbance 40
  - Difficulty concentrating 31
  - Skin rash 30
  - Diarrhea 18
  - Depression 22

# PGI--CCEP data

- Exposures: %
  - Diesel/other fuels 88
  - Pyridostigmine br 74
  - Oil well smoke fires 71
  - Insect repellents 66
  - Anthrax vaccine 49*
  - Botulinum vaccine 26**

** known to have been given to 21%; ** known to have been given to 1.1%*

# PGI--CCEP data Results

- No defined new syndrome
- If anyone would have such a syndrome, it would be in these self-referred service members (same with VA Registry)
- The meaning, evaluation, and treatment of these poorly defined symptoms needs further investigation (otherwise, doomed to repeat this after every war, as before)

# PGI--Features

- No single case definition would/will fit. If group sx, still no defined syndrome.
- Great difficulty has been lack of objective findings which, together with sx, would categorize into known syndromes

- ***Early decision when this was obvious: eligibility for care/disability need not depend on a case definition***

# The plural of anecdote is anecdotes, not data.

Marv Turck, M.D.

*Editor, J.I.D., traditional*

# PGI--Population-based studies

- Attempts to define characteristic morbidities/mortalities associated with PG deployment.
- Multiple studies
  - **Uncontrolled (Iowa)—soft findings (still self-selected)**
  - **Controlled (CCEP, UK)—no differences between groups**

# PGI--Has this been seen before?*

- Superb review highlights frequent occurrence of troublesome, poorly defined syndromes, with great overlap with “PGI”, after previous American Wars

– *Hyams, Ann Int Med, 1996*

| Symptom | War and Illness | | | | | |
|---|---|---|---|---|---|---|
| | U.S. Civil War, Da Costa Syndrome | World War I, Effort Syndrome | World War II, Combat Stress Reaction | Vietnam, Agent Orange Exposure | Vietnam and Other Conflicts, Post-Traumatic Stress Disorder | Persian Gulf, Unexplained Illnesses |
| Fatigue or exhaustion | + | + | + | + | + | + |
| Shortness of breath | + | + | + | | + | + |
| Palpitations and tachycardia | + | + | + | | + | |
| Precordial pain | + | + | | | + | + |
| Headache | + | + | + | + | + | + |
| Muscle or joint pain | | | | + | + | + |
| Diarrhea | + | | + | + | + | + |
| Excessive sweating | + | + | + | | | |
| Dizziness | + | + | + | + | + | |
| Fainting | + | + | | | | |
| Disturbed sleep | + | + | + | + | + | + |
| Forgetfulness | | + | + | + | + | + |
| Difficulty concentrating | | + | + | + | + | + |

* A plus sign indicates a commonly reported symptom.

**Hyams KC et al, Annals Int Med 1996**

“You see what you want to see, and you hear what you want to hear”

Harry Nillson

*The Point,* ca. 1972

# PGI: Why can't it be identified?*

- *COVERUP. Not enough being done; tons of investigators are in on the conspiracy.*
  - Ignorant, insulting, or both
- *Hazardous exposures not being adequately investigated.*
  - Wrong way around to identify new syndrome: first, unusual or rare disease; then back to exposures (leishmaniasis)

**Hyams, Am J Epid, 1998*

# PGI: Why can't it be identified? (II)

- *A better understanding of relationship between stress and organic dz needed.*
  - Unidentified organic disorder not found. Tons of prior data on this relationship.

# Causality:

Association between the environment and disease (Hill, 1964)

- *Strength of association*
- *Consistency*. Repeated, many times, many settings
- *Specificity*. Doesn't occur outside this setting
- *Temporality*. Correct sequence.

# Causality: Association between the environment and disease (Hill, 1964)

- *Biological gradient*. Dose response
- *Plausibility*. Makes sense. Depends on biological knowledge of the day.
- *Coherence*. Association should not conflict with known facts about the disease.
- *Experiment*
- *Analogy*. Occasionally fair to extrapolate/compare

# PGI: Potential causes

- Toxic exposures
  - Oil fires; gas/petroleum fumes
  - Depleted uranium
  - Exposure to chem agents/bio agents
  - Toxic paints (CARC [chem agent resistant coatings])

# PGI: Potential causes

- Infectious illnesses
  - **Diarrhea: squashed early (as problem and as a cause of PGI)**
  - **Viscerotropic leishmaniasis (<40 total, 12 possibly present)--all within 2 y of return; no reports since**
  - **No biowarfare detected**
  - **No malaria, sandfly fever, HFs appeared**

# PGI: Potential causes

- Multiple immunizations
  - **Anthrax: most; botulinum--very few**
  - **ISG; dT; typhoid**
  - **Speculation regarding "perturbations" in immune system triggering poorly defined sx like fatigue.*  Needs data.**

*Rook, Lancet, 1997; Reiber, Arch Int Med, 1996

# PGI: Potential causes

- Chemical exposures (pyridostigmine, DEET, and/or permethrin)
  - **Animal (chicken/mouse) models at high doses suggest potentiation of neurotoxicity**
  - **Genetic variation of cholinesterases**
  - **Known chronic OP poisoning in humans is dissimilar**

# PGI: Potential causes

- Psychological disorders
  - Some PTSD inevitable--1/4 to 1/2 pretty sure
  - Data on abnormal baseline diathesis
  - Large body of data on relationship between depression/anxiety and physical sx, without findings, and physicians and patients unaware of dx

People tend to get sick if they are treated as if they are expected to be sick*

** Cope, Lancet, 1994; Haynes, NEJM, 1978; Roht, Am J Epidemiol, 1985*

# *Post-traumatic stress disorder

- “Characterized by exposure to traumatic experiences outside the range of normal human experience, intrusive thoughts and memories associated with the trauma, persistent avoidance of stimuli associated with the trauma, and persistent symptoms of increased arousal associated with the trauma”

# PGI: Potential causes

- Psychological disorders (II)
  - “PGI” largely indistinguishable from other multisystem sx complexes with few findings, such as CF, fibromyalgia, and somatiform disorders.

# PGI: (Some more novel) Potential causes

- Mycoplasmas--Nicolson
- Urinary bacteria--Hyman
- Sand dust--Al Eskan disease

- **Theories characterized by wide unacceptance, minimal/no data, “proprietary information”, sense of desperation**

# What did we (Federal medical system) do right?

- Refused to be pressured into labeling patients--would have worsened situation
- Pursued/pursuing  research and education
- Future conflicts:  better plans for data collection

# What did we (Federal medical system) do right (II)?

- Took care of our patients, no matter what, including disability support.  Even if, ultimately, “only stress” associated, they fought for the country and now are in trouble

# What did we do wrong?

- Poor tracking of SM's health, vaccine, exposure status
  - SM's and public don't care if this was difficult to impossible
- Shuffled/obfuscated in defensiveness early on—Americans and Brits

# PGI--Personal experience with Phase II CCEP

- ~30 patients total seen, ~1994-98
- 2-3 true malingerers
- 12-15:  had diagnosable physical complaint (TB scar on CXR; hepatitis; chronic prostatitis, etc.)

# PGI--Personal experience with Phase II CCEP

- 12-15:  no acute problems; frankly admitted they wanted to get registered, and/or couldn’t get in through TMC to a specialist for chronic problem(s)
- 2-3:  something really wrong with (was I fooled?)

# PGI--the Future

- If organic pathology/lesions are found, define small subsets in which specific exposures may have produced unrecognized clusters of disease (e.g., both DEET and pyridostigmine?); use controls, objective endpoints

# PGI—the Future (II)

- Take care of our patients.
  - Routine care
  - “PGI” centers:  Clin eval; pharm Tx; exercise; cognitive/behavioral Tx

    - *(Engel, Mil Med, 1998)*

# PGI--the Future (III)

- Fund more?
- Empiric TX?  No.
- Resist labels.
- Carefully document all epidemiologic features in future deployments, within limits of safety

# PGI
# Summary and Conclusions

- Symptoms have been reported in high incidence in deployed PG vets (esp high in NG/Reserve units).
- No clustering of symptoms has been seen with which a syndrome can be recognized and diagnosed.
- No difference in pattern of reported symptoms between PGW and prior wars

# PGI
# Summary and Conclusions

- If measures are insensitive, and a small subset of illness is present but undiagnosed, there may have occurred a novel syndrome, with multiple causal theories extant. None seem consistent with known exposures and illnesses.